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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,522	06/28/2001	Maria A. Glucksmann	381552001700	7750

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EXAMINER	
SWOPE, SHERIDAN	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 01/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/896,522	GLUCKSMANN, MARIA A.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this c mmunication appears n the c ver sheet with the corresp ndence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-3,6,8 and 23-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23,26,29,32,35 and 38* is/are allowed.

6)☒ Claim(s) *1,3,6,8,24,25,27,28,30,31,33,34,36,37,39 and 40* is/are rejected.

7)☒ Claim(s) *1,2 and 27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1002.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election of Invention I, Claims 1-3, 6, and 8 in their response of October 14, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's cancellation of Claims 4, 5, 7, and 9-22, amendment of Claims 1 and 6, and addition of new Claims 23-40 is acknowledged. Claims 1-3, 6, 8, and 23-40 are hereby considered on their merits.

Specification-Objections

The specification is objected to for failing to disclose the ATCC number of deposited vectors; see, for example, page 3, lines 7, 10, and 14. The ATCC number for all deposited vectors and cells should be disclosed.

The specification is objected to for having a blank space at the bottom of pages 36.

The specification is objected to because Reference 11 on the 1449 form received September 25, 2002 does not have authorship and References 7-9 do not have dates. Correction is required.

Claims-Objections

Claim 1 is objected to for lacking an "or" between "SEQ ID NO: 1" and "SEQ ID NO: 3" in 1a- line 2, 1b-line 2, and lf-line 1-2.

Claim 27 is objected to for not having a period (.) at the end.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the following reasons.

Claim 1d is indefinite in reciting "the plasmid deposited with the ATCC as Accession Number _____". It is obviously unclear which plasmid Claim 1d is reciting. Correction is required.

Claims 1 and 6 are indefinite in reciting "a nucleic acid molecule which encodes a naturally occurring allelic variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 2" (Claims 1e and 6c). It is unclear whether the allelic variant comprises SEQ ID NO: 2, the allelic variant is a variant of a polypeptide comprising SEQ ID NO: 2, or the allelic variant is a variant of SEQ ID NO: 2. Clarification is required. For purposes of examination, it is assumed that Claims 1e and 6c are meant to recite a nucleic acid molecule which encodes a naturally occurring allelic variant of SEQ ID NO: 2.

Claims 1 as well as Claims 6 and 8 are indefinite in the recitation of "hybridizes... under stringent conditions" and "hybridizes", respectively, as this term is unclear absent a statement of the conditions under which the hybridization reaction is preformed. Nucleic acids that will hybridize under some hybridization conditions, will not necessarily hybridize under different conditions. The hybridization conditions described on page 18 line 22- page 19, line 11 are only exemplary and do not define the conditions recited in Claims 1, 6, and 8.

Claims 2 and 3, as dependent from Claim 1, are rejected under 35 U.S.C. 112, second paragraph for the same reasons.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 6, and 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleic acid molecules of SEQ ID NO: 1 and SEQ ID NO: 3, or nucleic acids encoding the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for any nucleic acid molecule with 80% homology to SEQ ID NO: 1 or 3, any fragment of SEQ ID NO: 1 or 3, nucleic acids encoding any fragment of SEQ ID NO: 2, or any nucleic acid that hybridizes to SEQ ID NO: 1 or 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 1 is so broad as to encompass any nucleic acid molecule which (i) is at least 80% identical to SEQ ID NO: 1 or 3, (ii) comprises a fragment of at least 15 nucleotides of SEQ ID NO: 1 or 3, (iii) encodes a polypeptide comprising at least 15 residues of SEQ ID NO: 2, or (iv) hybridizes to SEQ ID NO: 1 or 3. The scope of this claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed

knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of SEQ ID NO 2 and the nucleotide sequences of SEQ ID NO 1 and 3.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claim 1 which, encompasses all nucleic acid molecules which (i) are at least 80% identical to SEQ ID NO: 1 or 3, (ii) comprise a fragment of at least 15 nucleotides of SEQ ID NO: 1 or 3, (iii) encode a polypeptide comprising at least 15 residues of SEQ ID NO: 2, or (iv) hybridize to SEQ ID NO: 1 or 3. The specification does not support the broad scope of Claim 1 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the activity of uridine kinase; (B) the general tolerance of the activity of uridine kinase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Since Claims 3, 6, and 8 further recite vectors, host cells and methods of expressing the nucleic acids of Claim 1, Claims 3, 6, and 8 are also rejected under 35 U.S.C. 112 first paragraph due to lack of enablement for the same reasons discussed above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of nucleic acid molecules encoding polypeptides with an enormous number of amino acid modifications of the uridine kinase of SEQ ID NOS 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1, 3, 6, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The invention (Claim 1d) appears to employ a novel plasmid "deposited with the ATCC as Accession Number _____". Since the plasmid is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmid sequences are not fully disclosed, nor have all the sequences required for its construction been shown to be publically available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the vector. The specification does not disclose a repeatable process to obtain the vector and it is not apparent if the DNA

sequences are readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;

2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

4. the deposit will be replaced if it should ever become inviable.

Claims 3, 6, and 8, as dependent from Claim 1, are rejected under 35 U.S.C. 112, first paragraph for the same reasons.

Claims 1, 3, 6, and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules which (i) are at least 80% identical to SEQ ID NO: 1 or 3, (ii) comprise a fragment of at least 15 nucleotides of SEQ ID NO: 1 or 3, (iii) encode a polypeptide comprising at least 15 residues of SEQ ID NO: 2, (iv) hybridize to SEQ ID NO: 1 or 3, or (v) is deposited with the ATCC as Accession Number _____. The specification does not contain any disclosure of the function of all DNA sequences in said genus. The genus of nucleic acid molecules that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only two species of the claimed genus, SEQ ID NO: 1 and 3, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1, 3, 6, 8, 24, 25, 27, 28, 30, 31, 33, 34 36, 37, 39, and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2003 (US20030104529; filing date January 21, 2000) or Drmanac et al/Hyseq Inc., 2003 (US20030073623; filing date January 20, 1999). Tang et al teach a polynucleotide, where said polynucleotide (i) comprises 968 nucleotides of SEQ ID NO: 1, (ii) comprises 834 nucleotides of SEQ ID NO: 3, (iii) has 100% identity with SEQ ID NO: 3, and (iv) encodes a peptide having 100% identity with SEQ ID NO: 2 (see enclosed alignments). Tang et al (US20030104529) also teach their polynucleotide in a vector, wherein the vector is contained in a host cell, including mammalian host cells [0097] and their polypeptide as a fusion protein [0085]. Drmanac et al/Hyseq Inc. teach a polynucleotide, where said polynucleotide (i) comprises 403 nucleotides of SEQ ID NO: 1, (ii) comprises 403 nucleotides of SEQ ID NO: 3, and (iii) encodes a peptide having comprising 134 amino acid residues of SEQ ID NO: 2 (see enclosed alignments). Drmanac et al/Hyseq Inc. (US20030073623) also teach their polynucleotide in a vector, wherein the vector is contained in a host cell, including mammalian host cells [0129] and their polypeptide as a fusion protein [0112]. The polynucleotides of Tang et al and Drmanac et al/Hyseq Inc. would hybridize to the complement of SEQ ID NO: 1 and SEQ ID NO: 3. Therefore, Claims 1, 3, 6, 8, 24, 25, 27, 28, 30, 31, 33, 34 36, 37, 39, and 40 are rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al, 2003 (US20030104529; filing date January 21, 2000) or Drmanac et al/Hyseq Inc., 2003 (US20030073623; filing date January 20, 1999).

Claims 1, 3, 6, 8, 24, 25, 27, 28, 30, 31, 33, 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Ho et al, 2003 (US6579708; filing date March 27, 2000). Ho et al teach a

polynucleotide, where said polynucleotide (i) comprises 556 nucleotides of SEQ ID NO: 1, (ii) comprises 556 nucleotides of SEQ ID NO: 3, (iii) has 99.8% identity with SEQ ID NO: 3, and (iv) encodes a peptide having 100% identity with SEQ ID NO: 2 (see enclosed alignments). Ho et al (US6,579,708) also teach their polynucleotide in a vector, wherein the vector is contained in a host cell and their polypeptide as a fusion protein that has uridine kinase activity (Example 3). The polynucleotide of Ho et al would hybridize to the complement of SEQ ID NO: 1 and SEQ ID NO: 3. Therefore, Claims 1, 3, 6, 8, 24, 25, 27, 28, 30, 31, 33, and 34 are rejected under 35 U.S.C. 102(e) as being anticipated by Ho et al, 2003 (US6579708; filing date March 27, 2000).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 36, 37, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al, 2003 in view of Ausubel, 1987. The teachings of Ho et al are described above. Ho et al do not teach their vector in mammalian host cells. However, using mammalian cells as hosts for recombinant polynucleotides is common in the art (Ausubel, 1987). It would have been obvious to a person of ordinary skill in the art to use the methods of Ausubel et al to use mammalian cells as host cells for the polynucleotides of Ho et al. Motivation to do so derives from the desire to express the mammalian protein encoded by the polynucleotide of Ho et al in a mammalian cell, where all the proper mechanisms for post-translational processing are present. The expectation of success is high as, expression of proteins in mammalian host cells is common

in the art. Therefore, Claims 36, 37, 39, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ho et al, 2003 in view of Ausubel, 1987.

Allowable Subject Matter

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 23,26,29,32,35 and 38 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.

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